

Remarks

Claims 41-51 are pending in this application.

Claim 41 is amended to remove the terms “prevention,” “in need of such treatment or prevention,” “prophylactically,” and “prodrug.” Claim 41 is also amended to recite, in part, the administration of “racemic or optically pure” didesmethylsibutramine. Support for this amendment can be found, for example, on page 6, lines 7-11 and page 7, line 31 – page 8, line 3 of the specification.

Claims 43-45 are amended to recite, in part, that the recited amount administered is the amount “per day.” Support for this amendment can be found, for example, on page 16, lines 14-19 of the specification.

Claims 42 and 50 are amended to recite that “optically pure” didesmethylsibutramine recited in claim 41 is (R)- and (S)- didesmethylsibutramine, respectively.

The title of this application is amended to more correctly reflect the subject matter recited by the pending claims upon the entry of the amendments presented herein. The Abstract is amended to remove the description of compositions, as discussed in more detail below. No new matter has been added.

Applicants respectfully submit that the pending claims are allowable for at least the following reasons.

A. The Objection of the Abstract Should Be withdrawn

On page 2 of the Office Action, the objection of the abstract of the disclosure is maintained because, according to the Examiner, “the present claims are not drawn to compositions.” (Office Action, page 2). However, Applicants respectfully point out that the abstract is a summary of the disclosure, not the claims.

However, as suggested by the Examiner, the abstract has been amended to remove the description of compositions, and a replacement abstract page is provided herein. In view of these amendments, Applicants respectfully request that the objection of the abstract be withdrawn.

B. The Rejections Under 35 U.S.C. § 112 Should Be Withdrawn

1. The Enablement Rejections

On pages 2-6 of the Office Action, claim 41-51 are rejected as allegedly not enabled. In particular, it is alleged, based on the Examiner's analysis of *Wands* factors, that the description does not enable the "prevention" of depression.¹ Although Applicants respectfully disagree, claim 41 has been amended to remove the recitation of "prevention" solely to expedite the prosecution of the present application. In view of the amendment, Applicants respectfully request that this rejection be withdrawn.

2. The Indefiniteness Rejection

On page 8 of the Office Action, claims 42 and 50 are rejected as allegedly failing to particularly point out and distinctly claim the subject matter of the invention. In particular, it is alleged that the limitations (R)-didesmethylsibutramine and (S)-didesmethylsibutramine recited by claims 42 and 50 have "insufficient antecedent basis ... in claim 41." (Office Action, page 8). In this regard, claim 41 has been amended to recite, in part, "racemic and optically pure" didesmethylsibutramine, and claims 42 and 50 have been amended to recite, in part, that the "optically pure didesmethylsibutramine" is "(R)-" or "(S)-didesmethylsibutramine," respectively. In view of the amendments, Applicants respectfully request that this rejection be withdrawn.

3. The Rejection of the Term "Prodrug"

On page 9 of the Office Action, claims 41-51 are rejected as allegedly not enabled and as allegedly indefinite. This rejection is based on the allegation that the "metes and bounds of the term [prodrug] cannot be precisely determined." (Office Action, page 9). Although Applicants respectfully disagree, the term "prodrug" has been removed from claim 41. In view of the amendment, Applicants respectfully request that this rejection be also withdrawn.

¹ It is noted that the Office Action indicates that the "specification provides no support for prevention of depression." (Office Action, page 3). However, based on the analysis of *Wands* factors set forth in the Office Action, Applicants assume that the rejection is in connection with the enablement requirement.

C. The Rejection Under 35 U.S.C. § 103 Should Be Withdrawn

On pages 6-8 of the Office Action, claims 41-51 are rejected as allegedly obvious over WO 94/00047 (“the ‘047 publication”), WO 94/00114 (“the ‘114 publication”), and Luscombe et al., *Neuropharmacology*, 28(2): 129-134 (1989) (“Luscombe”). In particular, the Examiner alleges that the claims are obvious based on her assertion that: 1) Young “teaches the importance of stereochemical purity in the field of pharmaceuticals where chirality is demonstrated”; and 2) Luscombe “teaches ... didesmethylsibutramine ... to be considerably more active than sibutramine.” (Office Action, pages 6-7). Applicants respectfully traverse this rejection.

Under current law, a prior art reference or references cannot render a claim obvious unless the PTO provides evidence that the reference or references meet a three-part test for *prima facie* obvious. To begin with, the prior art reference or references must provide “motivation, suggestion, or teaching of the desirability of making the specific combination that was made by the applicant.” *See In re Kotzab*, 217 F.3d 1365, 1370, 55 U.S.P.Q.2d 1313, 1316 (Fed. Cir. 2000); *Princeton Biochemicals, Inc. v. Beckman Coulter, Inc.*, 2005 WL 1355127, at *4, 75 U.S.P.Q.2d 1051, 1054 (Fed. Cir. 2005). Where one reference is relied upon by the PTO, there must be a suggestion or motivation to modify the teachings of that reference. *See In re Kotzab*, 217 F.3d at 1370, 55 U.S.P.Q.2d at 1316-17. Where an obviousness determination relies on the combination of two or more references, there must be some suggestion or motivation to combine the references. *See WMS Gaming Inc. v. International Game Technology*, 184 F.3d 1339, 1355, 51 U.S.P.Q.2d 1385, 1397 (Fed. Cir. 1999); *Princeton Biochemicals, Inc.*, 2005 WL 1355127, at *4, 75 U.S.P.Q.2d at 1054; *Teleflex, Inc. v. Ficosa North America Corp.*, 299 F.3d 1313, 1334, 63 U.S.P.Q.2d 1374, 1387 (Fed. Cir. 2002). Second, the prior art references cited by the PTO must suggest to one of ordinary skill in the art that the invention would have a reasonable expectation of success. *See In re Dow Chemical*, 837 F.2d 469, 473, 5 U.S.P.Q.2d 1529, 1532 (Fed. Cir. 1988); *Boehringer Ingelheim Vetmedica, Inc.*, 320 F.3d 1339, 1354, 65 U.S.P.Q.2d 1961, 1971 (Fed. Cir. 2003); *Noelle v. Lederman*, 355 F.3d 1343, 1352, 69 U.S.P.Q.2d 1508, 1516 (Fed. Cir. 2004). Further, “[b]oth the suggestion and the reasonable expectation of success ‘must be founded in the prior art, not in the applicant’s disclosure.’” *Noelle*, 355 F.3d at 1352, 69 U.S.P.Q.2d at 1515-16 (quoting *In re Vaeck*, 947 F.2d 488, 493, 20

U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991)). Finally, the PTO must show that the prior art references, either alone or in combination, teach or suggest each and every limitation of the rejected claims. *See Motorola, Inc. v. Interdigital Tech. Corp.*, 121 F.3d 1461, 1473, 43 U.S.P.Q.2d 1481, 1490 (Fed. Cir. 1997); *Litton Systems, Inc. v. Honeywell, Inc.*, 87 F.3d 1559, 1569, 39 U.S.P.Q.2d 1321, 1327 (Fed. Cir. 1996). These criteria must be satisfied with factual and objective evidence found in the prior art; an examiner's conclusory statements cannot form a basis for a *prima facie* case of obviousness. *See In re Sang-Su Lee*, 277 F.3d 1338, 1343-44 (Fed. Cir. 2002).

As it currently stands, claim 41 recites, in part, the treatment of depression using racemic and optically pure didesmethylsibutramine. Therefore, the rejection set forth in the Office Action is essentially premised upon the proposition that the treatment of depression using racemic didesmethylsibutramine would have been obvious over Luscombe.² Applicants respectfully point out that such is not the case.

In this regard, Applicants respectfully point out that, among others, no motivation for those of ordinary skill in the art to use didesmethylsibutramine for the treatment of depression would have been provided by Luscombe. This is because Luscombe clearly discloses that "the secondary and primary amine metabolites" of sibutramine exhibit similar *in vivo* pharmacological activity to the parent compound. (See Luscombe, Abstract and Table 1 on page 131). Thus, those of ordinary skill in the art reading Luscombe's disclosure would not have been motivated to use didesmethylsibutramine on the face of the disclosure that no difference in pharmacological activity *in vivo* is observed for didesmethylsibutramine. This is particularly true for the claimed method, which involves the administration of didesmethylsibutramine to a patient.³ Therefore, Applicants respectfully submit that no *prima facie* case of obviousness has been established by Luscombe.

² This is because the '047 and '114 publications are merely cited to show the alleged obviousness of the use of optical isomers. In other words, regardless of what the '047 and '114 publications disclose, the claimed use of didesmethylsibutramine cannot be obvious unless Luscombe renders the use of racemic didesmethylsibutramine obvious.

³ In this regard, Luscombe's disclosure that didesmethylsibutramine is reportedly more potent than the parent compound *in vitro* is irrelevant to the patentability of the claimed methods since *in vivo* activity is what matters when determining whether an agent should be "administered to a patient." Therefore, those skilled in the art would not have acquired any motivation whatsoever from Luscombe's disclosure of *in vitro* activity.

In addition, Applicants respectfully point out that the disclosures of the '047 and '114 publications do not add anything to the substance of the rejection. As the Examiner recognizes, the '047 and '114 publications disclose the use of optical isomers of the parent drug sibutramine. Applicants respectfully point out that regardless of what has been disclosed in the '047 and '114 publications with regard to the optical isomers of sibutramine, such disclosure has no specific bearing on the patentability of the claims directed to the use of didesmethylsibutramine and its optical isomers. For example, such disclosure does not provide any specific motivation for making and using optical isomers of didesmethylsibutramine because pharmacological properties of optically pure sibutramine do not necessarily provide any indications as to those of optically pure didesmethylsibutramine. (*See, e.g., In re Grabiak*, 769 F.2d 729, 731 (Fed. Cir. 1985) (“Generalization should be avoided insofar as specific chemical structures are alleged to be prima facie obvious one from another.”); *see also Yamanouchi Pharm. Co., Ltd. v. Danbury Pharmacal, Inc.*, 231 F.3d 1339, 1343 (Fed. Cir. 2000) (“a prima facie case of obviousness requires structural similarity between claimed and prior art subject matter ... where the prior art gives reason or motivation to make the claimed compositions .”) (emphasis added)).

For at least the foregoing reasons, Applicants respectfully submit that no *prima facie* case of obviousness has been established by the references cited by the Examiner, and thus, request that the rejection of the claims be withdrawn.

D. The Rejection Under 35 U.S.C. § 102(b) Should Be Withdrawn

On page 8 of the Office Action, the rejection of claims 41, 46 and 47 as allegedly anticipated by Scott *et al.*, *Br. J. Pharmacol.*, 111: 97-102 (1994) (“Scott”) is maintained. Applicants respectfully traverse.

As well-settled, “[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.” (*Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987)). Scott reports the results of investigation regarding “the effects of [didesmethylsibutramine] ... on the responses evoked by visual stimulation and ionophoretic application of noradrenaline, 5-hydroxytryptamine, and excitatory amino acids in the rat dorsolateral geniculate nucleus.” (Scott, Abstract). Scott,

however, does not disclose "a method of treating depression comprising administering racemic or optically pure didesmethylsibutramine to a patient," as recited by claim 41. Therefore, as Scott fails to disclose "each and every element as set forth in the claim," Applicants respectfully submit that the claims are not anticipated by Scott, and thus, respectfully request that the rejection be withdrawn.

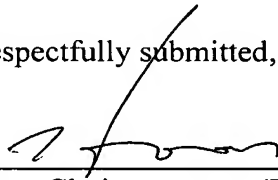
Conclusion

For at least the foregoing reasons, Applicants respectfully submit that all of the pending claims are allowable, and request that the rejection of the claims be withdrawn.

No fee is believed due for this submission. Should any additional fees be due for this submission or to avoid abandonment of the application, please charge such fees to Jones Day Deposit Account No. 503013.

Respectfully submitted,

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